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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,178	07/15/2003	Karel De Bruijn	4-30602B-D1	8650

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
DELACROIX MUIRHE, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,178	DE BRUIJN ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46-47, 52* is/are allowed.

6)☒ Claim(s) *27-45 and 48-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. Claims 27-45, 48-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/22340 ('340) in view of Giger et al., 5,510,353.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment(s)/Remarks

The following is responsive to applicant's remarks received March 23, 2006.

No claims are cancelled. No new claims are added. Claims 27-52 are currently pending.

Applicant's arguments traversing the previous claim rejection under 35 USC 103(a), set forth in paragraph 1 of the office action mailed Sep. 23, 2005, have been considered but are not found to be persuasive.

Said rejection is maintained essentially for the reasons given previously in the office action mailed Sep. 23, 2005 with the following additional comment.

Applicant contends that the WO '340 reference, either alone or in view of the '353 patent does not disclose or fairly suggest the claimed invention. Specifically, applicant argues that WO '340 discloses a rapid-release formulation of tolfenamic acid. This rapid release is achieved through the use of a superdisintegrant and by using particles with a mean particle size of < 10 microns. (See WO '340, page 3, lines 7-14.) The desired rapid-release properties are derived from the fact that the tablets contain smaller particles which will dissolve more quickly and through the use of superdisintegrants causing the tablet to disintegrate rapidly. The WO '340 publication also discloses that tolfenamic acid is useful for the treatment of patients suffering

from rheumatic diseases and that tolfenamic acid products are marketed for use as anti-inflammatory, analgesic agents, and anti-migraine agents. (WO '340, page 1, lines 11-24.) There is not indication anywhere in the WO '340 reference that tolfenamic acid is an acid sensitive agent. Accordingly, WO '340 does not disclose or suggest each and every element of the currently pending claims.

Moreover, applicant argues the motivation or suggestion to combine references in the manner suggested by the examiner must come from the references. There is no disclosure, direction or motivation in either reference to suggest the combination asserted in the Office Action. The '353 patent is directed to aminoguanidine compounds and their use in treating patients with gastrointestinal motility disorder or disorders associated with cephalic pain. There is no motivation for one skilled in the pharmaceutical formulation arts trying to over come the issues associated with the use of acid sensitive drugs, as claimed in the present application, to turn to the WO '340 application which is directed to the formulation of rapidly-disintegrating tablets and which is not directed to overcoming the problems associated with acid sensitivity. Further, there is no indication in WO '340 that tolfenamic acid would be useful as an agent for the treatment of gastrointestinal motility disorders or disorders associated with cephalic pain. Accordingly, there is no motivation or suggestion in either of the cited references to combine them in the manner suggested in the Office Action to produce the presently claimed invention. The rejection, therefore, should be withdrawn.

Said arguments have been considered but are not found to be persuasive.

The Examiner respectfully maintains that the claims are obvious in view of WO '340 and USPN '353. First of all, the examiner agrees with applicant that obviousness analysis requires

some motivation, suggestion or teaching, in the prior art, of the desirability of the invention. However, the examiner respectfully submits that express motivation is not required in order to modify or combine prior art. According to MPEP 2144, "[t]he rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). See also In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) (setting forth test for implicit teachings); In re Nilssen, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) (references do not have to explicitly suggest combining teachings); Ex parte Clapp, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985) (examiner must present convincing line of reasoning supporting rejection); and Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (reliance on logic and sound scientific reasoning)." The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2143.02.

In the present application, the claimed invention is drawn to a solid oral pharmaceutical composition comprising an acid sensitive agent and a disintegrant which is present in an amount of at least 15% by weight based on the total weight of the composition, wherein the disintegrant is a member selected from the group consisting of crospovidone, sodium starch glycolate, carboxymethylcellulose sodium, sodium alginate, and a mixture thereof. WO '340 discloses a tablet composition comprising tolfenamic acid (hydrophobic compound), alginic acid and at least

6% by weight of a superdisintegrant such as crospovidone, sodium starch glycolate and carboxymethylcellulose. WO '340 additionally teach that the amount of superdisintegrant will preferably not exceed 15-20% by weight as normally no particular benefits will be achieved beyond this range. (Please see page 3, line 7 to page 4, line 3; page 5, lines 32-34; page 7, lines 1-3).

The difference between the claims and WO '340 is that WO '340 discloses that the active ingredient is tolfenamic acid and not the claimed serotonergic compound, which is an acid sensitive agent. However, the examiner maintains it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the rapid release pharmaceutical composition of WO '340 to contain the serotonergic compound (3-(5-methoxy-1H-indol-3-yl-methylene)-N-pentylcarbazimidamide or salts thereof, a known pharmaceutical as taught by USPN '353, because WO '340 discloses that the tablet composition is capable of rapid release of the active ingredient (page 1, lines 5-8; page 2, lines 32-35) and one of ordinary skill in the art would *reasonably expect* the resulting tablet composition to rapidly release (3-(5-methoxy-1H-indol-3-yl-methylene)-N-pentylcarbazimidamide or salts thereof thereby decreasing the amount of time required to render a therapeutic effect.

The examiner also respectfully submits that a rationale or motivation to combine references which is different from that of applicant's is permissible under 35 USC 103(a) in supporting an obviousness rejection. Again the examiner refers applicant to MPEP 2144 where it is stated that "[t]he reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or *to solve a different problem.* It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by

applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991) (discussed below). Although Ex parte Levengood, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done" (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention. In this case, the examiner respectfully submits there is no requirement that the prior art, i.e. WO '340 and USPN '353, suggest the combination to address the problems associated with acid sensitivity, as proffered by applicant.

Furthermore, the Federal Circuit has held "[t]he strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination." In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Please also see MPEP 2144. The advantage or expected beneficial result from the combination of WO '340 and USPN '353 would be a solid oral pharmaceutical composition containing (3-(5-methoxy-1H-indol-3-yl-methylene)-N-pentylcarbazimidamide or salts thereof as the active agent, which upon administration to a patient in need thereof, effectively delivers the agent through a rapid release "mechanism" thereby quickly achieving a desired therapeutic effect. That is to say, upon administration to a patient suffering from cephalic pain, for example, the expected beneficial

result of the rapid release composition is that the desired analgesic effect would be achieved within a short period of time.

The rejection is respectfully maintained.

Allowable Subject Matter

Claims 46-47, 52 are free from the prior art because the prior art does not disclose or fairly suggest the claimed pharmaceutical composition.

Conclusion

Claims 27-45, 48-51 stand rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ardin Marschel**, can be reached on **571-272-0718**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
June 8, 2006

Ardin U. Marschel 6/11/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER